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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,115	08/31/2005	Martin Hendrix	01-2112	5580

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EXAMINER	
MURRAY, JEFFREY H	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
07/22/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO.e-Office.rdg@boehringer-ingelheim.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,115	HENDRIX ET AL.	
	Examiner	Art Unit	
	JEFFREY H. MURRAY	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,9,13,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *1-5,7 and 13* is/are allowed.

6)☐ Claim(s) *9 and 15* is/are rejected.

7)☐ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/25/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-5, 7, 9, 13, 15 and 16 are pending in this application. Claims 6, 8, 10-12 and 14 have been cancelled. This action is in response to the applicants' request for a continued examination filed on June 25, 2010.

Withdrawn Rejections/Objections

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

Claim Rejections - 35 USC § 112, 1st paragraph

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the inhibition of PDE 9A *in vitro*, does not reasonably provide enablement for treating an impairment of learning and/or memory which is a consequence of Alzheimer's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicants have argued in a past action that there is a nexus between the testing they have performed in the specification and a use in carrying out the claimed methods. They point specifically to a document Van der Staay, Neuropharmacology, vol. 55, pp. 908-918 (2008) to strengthen their belief that there is a nexus. Unfortunately, the specification of an application must be enabling as of the filing date (see MPEP 2164.05(a)) thus any published documents supporting the concept of enablement must

be dated on or before the filing date of the current application. Here, the Van der Staay document is accepted on July 4, 2008, while the application was originally filed in 2005, thus the document, as well as the arguments used by the applicants referencing this document, can not be used to assist in teaching enablement of the current invention. This also holds true for other documents and references used to show enablement within the applicants' arguments such as Reymann et. al. (2007); Wunder et. al. (2005); and Lugnier, et. al. (2006).

Contrary to the applicants' previous assertion on page 11 as to "providing no evidence to support why it doubts the truth or accuracy of the inventor's statements…" The examiner has provided documentation and discussed the aspects of the claims at length in a previous rejection. Particularly mentioned was the fact that many kinds of therapies have been investigated in the past, including Hydergine-LC (actually approved by the FDA for Alzheimer's Disease, but later determined to make the disease worse), Cu/Zn chelators (or Cu and Zn homeostasis regulators), endothelin B receptor agonists, α-TNF inhibitors, angiotensin II receptor antagonists, ACE inhibitors, EAA agonists (including partial agoinists), estrogens, metabotropic receptor agonists, muscarinic M2 receptor antagonists, free-radical scavengers, butyrylcholinesterase inhibitors, cholinergic agonists, potassium-channel blockers, P38 kinase inhibitors, sigma-1 Receptor Agonists, 5-HT1A receptor antagonists, α secretase stimulants, and others.

From this immense body of work, only two kinds of drugs ever emerged. Four Acetylcholinesterase inhibitors were found to have some limited value: tacrine (Cognex®, no longer clinically used); donepezil (Aricept®); galantamine

(Razadyne®/Reminyl®/Nivalin®) and rivastigmine (Exelon®). In addition, one voltage-dependent NMDA-antagonist, Memantine (Axura®/Akatinol®/Namenda®/Ebixa®) was also found effective. Categories of agents and techniques under investigation as of 2010 include Aß aggregation inhibitors, assorted antioxidants, γ-Secretase modulators, γ-Secretase inhibitors, NGF mimics, PPAR agonists, HMG-CoA reductase inhibitors (statins), Ampakines, Calcium channel blockers, GABA receptor antagonists, Glycogen synthase kinase inhibitors, Intravenous immunoglobulin, Muscarinic receptor agonists, cholinesterase inhibitors, Nicotinic receptor modulators, Passive Aß immunization, Serotonin receptor antagonists, Active Aß immunization, NGF gene therapy, H_3-receptor antagonists, NSAIDs (including NO-NSAIDs and COX-2 Inhibitors), and CB_1 and CB_2 cannabinoid receptor agonists. It is or course entirely possible that one or more of these will eventually be made to work. However, as can be seen by the many, many categories of drugs which never panned out, simply being the subject of active investigation is no indication that enablement is present at that time. The skill level in this art is so low that only Acetylcholinesterase inhibitors and NMDA-antagonists have been made to work.

Finally, there are several types of dementia, some of which are often confused with Alzheimer's disease, such as Multi-Infarct dementia (MID). Multi-infarct dementia (MID) is the second most common cause of dementia (after Alzheimer's disease) in people over age 65. (http://www.nlm.nih.gov/medlineplus/ency/article/000746.htm, last accessed July 15, 2010) As several of the symptoms are identical to dementia caused by Alzheimer's disease, it would be impossible to determine if a treatment was treating

"an impairment of learning and/or memory which is a consequence of Alzheimer's Disease" (as per claim 9) or whether the treatment was treating a type of dementia which is not caused by Alzheimer's disease. An additional complication is that there is no good physiological test for determining if one has Alzheimer's Disease; one must rely on assorted psychological tests. A definitive diagnosis of Alzheimer's Disease can only be done post mortem. No new matter permitted. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Applicants claim a "method for producing a medicament…" yet there are no method steps present. No new matter permitted. Appropriate correction required.

Claim 15 is rejected under 35 U.S.C. 112,second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of an intended use, chemical activity, or functional description of some "additional" property for a compound (or moiety/functionality attached to a chemical core) or a composition containing same, must result in a tangible structural difference between the product of that claim and of the product set forth in the copending claim. In the absence of said structural difference between the products of

the copending claims, said claim is seen to be a substantial duplicate, and said recitation is not afforded critical weight and fails to further limit the product in said dependent claim. In the instant set of claims, claim 15 merely "provides a compound of Formula (I)" and thus fails to further limit Claim 1.

Double Patenting

Claim 16 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Examiner notes that the pharmaceutical composition does not contain any further limiting factors from claim 1, (for example, an inert carrier or adjuvant). By listing only the same compound limitations as claim 1, the pharmaceutical composition is a substantial duplicate of claim 1. No new matter permitted. Appropriate correction required.

Allowable Subject Matter

Claims 1-5, 7 and 13 are allowed.

Claims 1-5, 7, 9 and 13 are free of the prior art. The closest prior art to the claims is Miyashita, et. al., Heterocycles (1990), 31(7), 1309-14. Miyashita, et. al. however, teaches a phenyl ring in the R^2 position, not a cycloalkyl group, and also teaches an unsubstituted phenyl ring for R^1.

Conclusion

Claims 9 and 15 are rejected.

Claim 16 is rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/
Patent Examiner , Art Unit 1624